Remarks

Claims 1-10 and 12-27 are pending. Claim 11 was previously canceled without prejudice. Claim 21 is hereby canceled, without prejudice, only because claim 1, as amended, and claim 21 have identical limitations even though they are written differently. Claims 1-6, 9-10, 12-17 and 19-25 are currently amended. Support for the phrase "synthetic peptide factor" in amended claims 1-6, 9-10, and 19-25 is found in paragraphs [0001], [0006], [0021], [0032], [0043], [0050], [0061] and [0076]. Support for addition of the phrase "having the sequence of SEQ ID NO:2" or "having SEQ ID NO:2" in amended claims 1, 5, 6, 19, 20, 21, 24 and 25 is found in paragraphs [0015], and [0043]. Support for the phrase "or both of i) SEQ ID NO:2 tyrosine amino acid residue 5 and ii) SEQ ID NO:2 arginine amino acid residue 9 are substituted with a tyrosine analog or arginine analog, respectively" of amended claims 1, 5 and 6 is found in paragraph [0017] and Table 1a. Support for SEQ ID NO:2 in claims 1, 3-6, 9-10, 13-14, 16-17, and 19-25 is found in paragraph [0015], and [0043]. Amendments of claims 1, 5, 6, 19, 20, 24 and 25 to recite "said sequence" are done only to reflect more accurately the relationship of the sequence and the synthetic peptide. Amendments to claims 1, 19 and 20 to recite "capable of binding to" are made only to reflect more accurately the relationship of the claimed composition and the laminin receptor. Amendments to claims 2, 12, 15, 19, 20, 24 and 25 regarding the N-terminal and C-terminal amino acid residue phrases are only made to more accurately reflect the relationship between the N-terminal and C-terminal amino acid residues and modifications. Typographical errors over the placement of hyphens have been corrected in claims 2, 12, 15, 19, 20, 24 and 25. Typographical errors over the placement of a comma have been corrected in claims 2, 12, and 15.

Response to rejection of Claims 1-4, 9, 10 and 19-23 under 35 U.S.C. § 101.

The Examiner rejected claims 1-4, 9, 10 and 19-23 under 35 U.S.C. § 101 as directed to non-statutory subject matter because the recited "peptide factor" does not indicate the hand of man. The claims, as supported by the specification, are directed to a modified or synthetic peptide, and thus are directed to statutory subject matter. However, in an earnest effort to advance the claims toward allowance, Applicants hereby amend the subject claims. The subject claims, as amended, recite a "synthetic peptide factor," thus indicating the hand of

man. Therefore, the Examiner's rejection under 35 U.S.C. § 101 is presumed to be overcome.

Response to rejection of Claims 1-10 and 12-27 under 35 U.S.C. § 112, first paragraph, enablement.

The Examiner rejected the subject claims for lack of enablement due to the number of possible Tyr or Arg modifications rectied in the claims. The Examiner admits that modification of m-EGF at the tyrosine or the arginine of SEQ ID NO:2, with a tyrosine analog or a arginine analog, respectively, is enabled. The Examiner stated:

> [T]he specification, *while being enabling for* a peptide factor (m-EGF, SEQ ID NO:2) having *tyrosine substituted with a tyrosine analog, or arginine substituted with an arginine analog*[.]

(Office Action at point 6, pages 3-4. Emphasis added.). It is clear from the Examiner's statement that the Examiner found that claims reciting modification of a tyrosine or an arginine are enabled. Claim 1, as amended, recites, in part:

> A synthetic peptide factor comprising amino acid residues 33 to 42 of murine epidermal growth factor having the sequence of SEQ ID NO:2 wherein:
>
> a) said sequence is modified such that at least one or both of i) SEQ ID NO:2 tyrosine amino acid residue 5 and ii) SEQ ID NO:2 arginine amino acid residue 9 are substituted with a tyrosine analogue or arginine analogue, respectively[.]

All other independent claims (5, 6, 19-21, 24 and 25) are similarly, if not identically, amended. One of ordinary skill in the art would readily understand which positions of SEQ ID NO:2 are to be modified from the direct language of the claim. Additionally, one of ordinary skill in the art would readily understand that any tyrosine or arginine analog is contemplated from paragraphs [0022]-[0026], [0030] and [0095] of the specification. Since the specification, as admitted by the Examiner, supports modification of positions 5 and 9 of SEQ ID NO:2 with a tyrosine or arginine analog, the specification adequately supports claims directed to those modifications. Therefore, claims 1-10 and 12-27 are enabled for the modification of tyrosine amino acid residue 5 and arginine amino acid residue 9 within SEQ ID NO:2 of a synthetic peptide with a tyrosine or arginine analog, respsectively. Therefore,

Examiner's rejection of the subject claims as non-enabled due to substitution of "at least one" tyrosine or arginine is presumed to be overcome.

The Examiner rejected claims 1-10 and 12-27 as not enabled for synthetic peptides "where more modifications other than substitutions at Try or Arg of residues 33 to 42 of mEGF are not identified." However, the Examiner admits that claims encompassing more modifications other than substitutions at Tyr or Arg are enabled. The quote of the Examiner given above, expanded to include the previously excised portions, states:

> [T]he specification, *while being enabling for* a peptide factor (m-EGF, SEQ ID NO:2) having tyrosine substituted with a tyrosine analog, or arginine substituted with an arginine analog, and optionally having N-terminal residue, C-terminal residue or cysteine thiol group capped, or, replacement of a peptide bond with a protease-resistant peptide bond isostere, replacement of a glycine residue with α,α-dialkyl substituted amino acid, or stabilization of a helical turn of the peptide using intra chain linkers; or a method of agonizing or antagonizing a laminin receptor comprising administering to a patient a medicament comprising the peptide factor[.]

(Office Action at point 6, pages 3-4. Emphasis added.) The only substantive difference between what the Examiner found to be enabled and what the Examiner found to be non-enabled is the number of tyrosine residues or arginine residues that can be substituted. The Examiner included every "modification other than substitutions at Tyr or Arg of residues 33 to 42 of mEGF" possible for a claimed synthetic peptide in the list of modifications that the Examiner found enabled. Since the Examiner finds all possible claimed modifications of synthetic peptides enabled, but then proceeds to reject the claims for inclusion of those modifications, the Examiner has provided an unreasonable basis for an enablement rejection. Therefore, the Examiner has not carried the Examiner's burden of establishing a reasonable basis for an enablement rejection under § 2164 of the Manual of Patent Examining Procedure ("MPEP").

Nonetheless, Applicants address each of the Examiner's points for rejecting the subject claims as non-enabled right after finding them enabled. The Examiner discussed the breadth of the claims, the absence or presence of working examples, the state of the prior art, predictability of the art, the amount of guidance necessary, and the nature of the invention.

Breadth of claims: The Examiner stated that the subject claims are "broad and encompass unspecified variants ... not adequately described or demonstrated in the

specification." The claims may encompass a number of modified synthetic peptides, but one of ordinary skill in the art would readily understand the boundary of the kinds of synthetic peptide modifications given the language in the claims and the supporting specification. When a composition is limited to a particular use, the claim should be evaluated on the basis of that use. MPEP § 2164.01(c). Each subject independent claim provides a list of modifications possible. For example, claim 19, with the most extensive set of modifications possible, recites, in part:

> ...wherein said first modification is selected from the group consisting of: substitution of SEQ ID NO:2 tyrosine amino acid residue 5 with a tyrosine analogue and substitution of SEQ ID NO: 2 arginine amino acid residue 9 with an arginine analogue; and
>
> wherein said second modification is selected from the group consisting of: chemical modification of the N-terminal amino acid residue of the murine epidermal growth factor by the addition of an amino acid capping moiety; chemical modification of the C-terminal amino acid residue of the murine epidermal growth factor by the addition of an amino acid capping moiety; chemical modification of a murine epidermal growth factor cysteine residue thiol group by the addition of an amino acid capping moiety to the cysteine residue thiol group; replacement of a peptide bond with a protease-resistant peptide bond isostere, replacement of a glycine residue with αα-dialkyl substituted amino acid; and stabilisation of a helical turn of the peptide using suitable intra chain linkers.

The list of said second modification includes, and is limited to, only six kinds of modifications. Each claim also demands that the synthetic peptide interact with the laminin receptor in step b. One skilled in the art could readily synthesize the synthetic peptide with six kinds of modifications and test the synthetic peptide for binding or interaction with laminin receptors as provided in paragraphs [0045] (peptide synthesis) and [0061]-[0072] (tests). Given that one of ordinary skill in the art, with the teachings of the specification, could readily synthesize and test every claimed modified synthetic peptide for interaction with a laminin receptor, the breadth of the claims is not overly broad.

Absence or presence of working examples: The Examiner stated that there are no working examples. However, every paragraph [0083]-[0098] is a result of actual experiments outlined in paragraphs [0061]-[0082]. Within paragraphs [0083]-[0098], numerous working examples are presented to show how specific modifications of the claimed synthetic peptide factor sequence affect interactions of the synthetic peptide with laminin receptors. For

example, paragraph [0090] relates the effects of alanine substitution in the synthetic peptide. Additionally, paragraph [0096] teaches that H-bonding across peptide bonds is important in determining antagonistic activity. The specification does not list a working example for every modification recited in the subject claims, however, there is no requirement that any working example be present in order to enable claims. MPEP § 2164.02. Since there are many working examples for many of the six kinds of modifications claimed, one of ordinary skill in the art would readily be able to adapt the working examples to test the claimed modifications for which there are no working examples.

State of the prior art: The Examiner stated that the state of the prior art does not supplement the "omitted description." The Examiner goes on to request specific teachings on identities of modified peptides containing more modifications ... and the effects of these peptides in agonizing or antagonizing a laminin receptor. Since the Examiner admits that the modifications contemplated are enabled by the specification, as in the quote above, there is no need for prior art to supplement the "omitted description."

Predictability of the art, the amount of guidance necessary, and the nature of the invention: The Examiner stated that the invention "is highly unpredictable regarding the effects of various modified peptide factors in agonizing or antagonizing a laminin receptor." However, the amount of guidance required in a specification is inversely proportional to both the level of skill in the art and the predictability in the *art*, not the *invention*. MPEP § 2164.03. In this case, the level of ordinary skill in the art of synthetic peptide binding to laminin receptors is high. Since the specification exhaustively describes how to synthesize and test a synthetic peptide (paragraphs [0045] and [0061]-[0072] respectively) with the modifications claimed, one of ordinary skill in the art would readily be able to conduct and interpret the synthesis and tests of a synthetic peptide as claimed. Therefore, any unpredictability in the art is ameliorated by the high level of skill in the art combined with the exhaustive list of how to synthesize and test the claimed synthetic peptide. These arguments are equally applicable to the Examiner's statements regarding the amount of guidance necessary and the nature of the invention as well.

In conclusion, one of ordinary skill in the art would not find the claims over-broad, would not need more working examples above the numerous ones provides, and would not need further guidance to apply the teachings of the specification in order synthesize and test

synthetic peptides as recited in the subject claims. Since the specification exhaustively describes how to synthesize and test every claimed synthetic peptide, the specification teaches how to make and use the claimed synthetic peptides without undue experimentation. Therefore, the subject claims, as amended, are enabled under 35 U.S.C. §112, first paragraph.

Response to rejection of Claims 1-10 and 12-27 under 35 U.S.C. § 112, second paragraph, indefinite.

The Examiner rejected claims 1-10 and 12-23 as indefinite because the claims recited amino acids 33 to 34 of murine epidermal growth factor without providing a reference sequence identification number. The specification as filed supports the recitation of amino acids 33 to 42 of murine epidermal growth factor. However, in an earnest effort to advance the claims toward allowance, Applicants hereby amend all subject claims to recite SEQ ID NO:2. Therefore, the Examiner's rejection is believed to be overcome.

The Examiner rejected claims 1-10 and 12-23 as indefinite for not clarifying that the murine epidermal growth factor peptide, with the recited modifications, is the "factor that binds to laminin receptors in step b)" All of the independent claims are hereby amended to recite "said sequence is modified" in step 'a' to reflect more accurately the relationship of the sequence and the synthetic peptide factor. Since the claims clearly indicate that it is the synthetic peptide, with sequence modifications recited in step 'a', that binds to the laminin receptor, the claims are definite. Therefore the Examiner's rejection is believed to be overcome.

The Examiner rejected claims 19-27 as indefinite for including an open ended clause in a Markush group. Claim 19, as amended, recites "...the group consisting of: substitution of SEQ ID NO:2 tyrosine amino acid residue 5 with a tyrosine analogue and substitution of SEQ ID NO: 2 arginine amino acid residue 9 with an arginine analogue...." Claims 20, 24, and 25 are similarly amended. Claims 22-23 are dependent on claim 19, and therefore incorporate the amendments through dependency. Claim 21 is canceled for other reasons. Since the claims, as amended, no longer contain an open ended clause in a Markush group, the Examiner's rejection is believed to be overcome.

Conclusion

Based on the foregoing, all claims are believed to be in condition for allowance. An early and favorable action toward that end is earnestly solicited.

Respectfully submitted,

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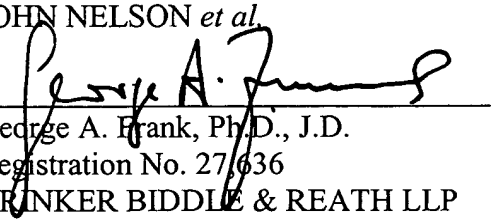

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